Pharmacy Medical Policy
Supportive Care Treatments for Patients with Cancer

Policy Number: 105
BCBSA Reference Number: None

Related Policies
- Quality Care Dosing guidelines apply to the following medications and can be found in Medical Policy #621
- Blue Cross Blue Shield of Massachusetts’ Medicare HMO Blue and Medicare PPO Blue Formulary

Table of Contents
Overview ........................................................................................................................................... 1
Policy ............................................................................................................................................... 2
Medicare Advantage (HMO Blue and PPO Blue) Part D Pharmacy Benefit Coverage Criteria .......... 2
Commercial Managed Care (HMO and POS), Commercial PPO/EPO and Medicare Advantage (HMO
Blue and PPO Blue) Part B Medical Benefit Coverage Criteria ....................................................... 3
Requesting Prior Authorization Information through Carelon Medical Benefits Management ............ 6
Requesting Prior Authorization Information through BCBSMA under Retail/Specialty Pharmacy .......... 6
Sources of Clinical Criteria for Review of Requests for Medicare ..................................................... 6
Individual Consideration .................................................................................................................. 7
CPT Codes / HCPCS Codes / ICD Codes ......................................................................................... 7
Policy History ................................................................................................................................. 7
References ........................................................................................................................................ 7

Overview
Effective July 1, 2021, BCBSMA has delegated Medical Utilization Management of Colony Stimulating
Factors to Carelon Medical Benefits Management (Carelon) for Commercial and Medicare Advantage
products.

The National Cancer Quality Program (NCQP) requires prior authorization for Colony Stimulating Factors
per the medical necessity criteria reflected in the Carelon clinical guideline below (Medical Claims only).

The Carelon Clinical Appropriateness Guidelines are based on peer-reviewed literature and
recommendations from evidence-based research centers such as (but not limited to): the American
Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN).
Note: Medicare Retail Pharmacy Part D claims are excluded from this program and should be directed to BCBSMA Pharmacy Operations Department at (800) 366-7778.

Policy
Commercial Managed Care (HMO and POS), Commercial PPO/EPO and Medicare Advantage (HMO Blue and PPO Blue)

Prior Authorization Information

<table>
<thead>
<tr>
<th>☒ Prior Authorization</th>
<th>☐ Step Therapy</th>
<th>☒ Quality Care Dosing</th>
<th>Pharmacy Operations:</th>
<th>To request for coverage: Physicians may call, fax, or mail the attached form (Formulary Exception/Prior Authorization form) to the address below.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tel: 1-800-366-7778</td>
<td>Blue Cross Blue Shield of Massachusetts Pharmacy Operations Department 25 Technology Place Hingham, MA 02043</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fax: 1-800-583-6289</td>
<td>Individual Consideration: Policy for requests that do not meet clinical criteria of this policy, see section labeled Individual Consideration</td>
</tr>
</tbody>
</table>

Pharmacy (Rx) or Medical (MED) benefit coverage

| ☒ Rx | ☒ MED |

Policy applies to Commercial Members:
- Managed Care (HMO and POS), PPO and Indemnity
- MEDEX with Rx plan
- Managed Major Medical with Custom BCBSMA Formulary
- Comprehensive Managed Major Medical with Custom BCBSMA Formulary
- Managed Blue for Seniors with Custom BCBSMA Formulary

Please refer to the chart below for the formulary status of the medications affected by this policy.

The following Medications may be approved when there is a contraindication or an adverse reaction to the use of TWO of the Preferred agents listed in the appropriate sections below: Nivestym ® (filgrastim-aafi), Nyvepria ™ (pegfilgrastim-apgf), Neupogen ® (filgrastim), Releuko ™ (filgrastim-ayow), Fynletra ® (pegfilgrastim-pbbk), Rolvedon ™ (eflapagratim-xnst), Stimufend ® (pegfilgrastim-fpgk) or Udenyca ™ (pegfilgrastim-cbqv) and relevant medical benefit (clinical appropriateness) criteria is met.

<table>
<thead>
<tr>
<th>Preferred Drug / Step 1</th>
<th>Status</th>
<th>Non-Preferred Drug / Step 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granix ® (Tbo-filgrastim)</td>
<td>PA required</td>
<td>Neupogen ® (filgrastim)</td>
</tr>
<tr>
<td>Zarxio ® (filgrastim-sndz)</td>
<td></td>
<td>Nivestym ™ (filgrastim-aafi)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Releuko ™ (filgrastim-ayow)</td>
</tr>
</tbody>
</table>
Continued from above

<table>
<thead>
<tr>
<th>Preferred Drug / Step 1</th>
<th>Status</th>
<th>Non-Preferred Drug / Step 2</th>
</tr>
</thead>
</table>
| Fulphila® (pegfilgrastim-jmdb)  
Ziextenzo™ (pegfilgrastim-bmez)  
Neulasta® / OnPro® (pegfilgrastim) | PA required   | Fylnetra® (pegfilgrastim-pbbk)  
Nyvepria™ (pegfilgrastim-apgf)  
Rolvedon™ (eflapegrastim-xnst)  
Stimufend® (pegfilgrastim-fpgk)  
Udenyca™ (pegfilgrastim-cbqv) |
| Leukine® (sargramostim)    | PA required   |                                                                 |

**Medicare Advantage (HMO Blue and PPO Blue) Part D Pharmacy Benefit Coverage Criteria**

To reference the criteria, click Blue Cross Blue Shield of Massachusetts' Medicare HMO Blue and Medicare PPO Blue Formulary.

**Commercial Managed Care (HMO and POS), Commercial PPO/EPO and Medicare Advantage (HMO Blue and PPO Blue) Part B Medical Benefit Coverage Criteria**

**Note:** Consideration should be given to equally effective and safe alternative chemotherapy treatment options that do not require colony stimulating factor (CSF) support, when available. All non-oncology diagnosis (i.e., Donor Medication use) will be reviewed by Blue Cross Blue Shield and can be found in Policy 033.

We may cover Fulphila® (pegfilgrastim-jmdb), Granix® (Tbo-filgrastim), Zarxio® (filgrastim-sndz), Ziextenzo™ (pegfilgrastim-bmez), and Neulasta (pegfilgrastim) for primary prophylaxis of febrile neutropenia when **ALL** of the following criteria are met:

- The individual has a **non-myeloid malignancy** and is NOT receiving chemotherapy with radiation concurrently; **AND**
- Chemotherapy intent must include **ONE** of the following:
  a. Curative intent (for example adjuvant treatment for early-stage disease), **OR**
  b. Intent is survival prolongation, and the **use of a different regimen or dose reduction would reduce the likelihood of reaching the treatment goal,** **OR**
  c. Intent is symptom management, and the **use of a different regimen or dose reduction would reduce the likelihood of reaching the treatment goal; AND**
- The individual falls into **ONE** of the following risk categories for febrile neutropenia:
  a. High risk of febrile neutropenia (≥ 20%) based on chemotherapy regimen risk (per Carelon Febrile Neutropenia Risk Guideline), **OR**
  b. Intermediate risk of febrile neutropenia (≥ 10% but < 20%) based on chemotherapy regimen risk (per Carelon Febrile Neutropenia Risk Guideline), and at least **ONE** of the following significant risk factors:
    I. Age > 65
    II. Poor performance status (ECOG 3 or 4, but chemotherapy still indicated)
    III. Preexisting neutropenia, for example resulting from bone marrow damage or tumor infiltration (ANC < 1500 mm$^3$)
    IV. Previous febrile neutropenia episode
    V. Liver dysfunction, with bilirubin ≥ 1.0 or liver enzymes ≥ 2x upper limit of normal
VI. Presence of open wounds or active infections, when chemotherapy cannot be delayed in order to accommodate recovery
VII. Renal dysfunction with creatinine clearance of less than 50 mL/min
VIII. Poor nutritional status (baseline albumin less ≤ 3.5 g/dL or BMI less than 20)
IX. HIV infection (active) requiring ongoing antiviral therapy
X. High tumor volume and/or high symptom burden from disseminated or unresectable malignancy
XI. Multiple serious comorbid conditions in addition to the treated malignancy.

We may cover Fulphila® (pegfilgrastim-jmdb), Granix® (Tbo-filgrastim), Zarxio® (filgrastim-sndz), Zielextenzo™ (pegfilgrastim-bmez), and Neulasta (pegfilgrastim) for secondary prophylaxis of febrile neutropenia when ALL of the following criteria are met:

Secondary prophylaxis of febrile neutropenia is considered clinically appropriate when there has been a previous neutropenic complication (in the absence of primary prophylaxis), and a change to the regimen (including dose reduction, schedule change, or change in therapy) would be expected to compromise patient outcome, particularly in the setting of curative intent.

We may cover Fulphila® (pegfilgrastim-jmdb), Granix® (Tbo-filgrastim), Zarxio® (filgrastim-sndz), Zielextenzo™ (pegfilgrastim-bmez), and Neulasta (pegfilgrastim) for adjunctive treatment of febrile neutropenia (primary prophylaxis not given) when ALL of the following criteria are met:

Adjunctive treatment of febrile neutropenia is considered clinically appropriate when ANY of the following risk factors are present (in the absence of prior growth factor use within the same cycle of treatment):
1. Age > 65
2. Neutrophil recovery is expected to be delayed (greater than 10 days)
3. Neutropenia is profound (less than 0.1 x 10^9)
4. Active pneumonia
5. Sepsis syndrome (hypotension and/or multi-organ damage/dysfunction noted)
6. Invasive fungal or opportunistic infection
7. Onset of fever during inpatient stay.

Note: Febrile neutropenia is defined as an oral temperature > 38.3°C (101.0°F) or 2 consecutive readings of 38.0°C (100.4°F) for 1 hour, with an absolute neutrophil count less than 500 cells/microL (0.5 x 10^9/L) or less than 1000 cells/microL and expected to fall below 500 cells/microL over the next 48 hours.

We may cover Granix® (Tbo-filgrastim), and Zarxio® (filgrastim-sndz) for the following indications by growth factor type when the requirements below are met:

1. Acute lymphocytic leukemia (ALL)
   a. After start of induction or first post-remission chemotherapy course; OR
   b. As an alternate or adjunct to donor leukocyte infusions (DLI) for relapsed disease after transplant
2. Acute myeloid leukemia (AML)
   a. After induction, reinduction, or consolidation; OR
   b. As an alternate or adjunct to donor leukocyte infusions (DLI) for relapsed disease after transplant
3. Aplastic anemia, moderate or severe
4. Hairy cell leukemia
   a. To treat severe neutropenia
5. Hematopoietic stem cell transplant
   a. To promote bone marrow myeloid recovery, OR
   b. To treat delayed or failed engraftment, OR
6. Myelodysplastic syndrome (MDS)
   a. To treat recurrent infection, OR
   b. To treat neutrophil count < 500 mm$^3$

7. Radiation exposure
   a. Following radiation therapy in the absence of chemotherapy, if prolonged delays are expected, OR
   b. After accidental or intentional body irradiation of doses greater than 2 Gy (hematopoietic syndrome of acute radiation syndrome)

8. Support for dose dense or dose intensive chemotherapy in ANY of the following scenarios:
   a. Adjuvant treatment of high-risk breast cancer with combination therapy that includes anthracycline (doxorubicin or epirubicin)/cyclophosphamide followed by paclitaxel, OR
   b. High-dose intensity methotrexate, vinblastine, doxorubicin, and cisplatin (HD-M-VAC) in urothelial cancer; OR
   c. Chemotherapy intensification for newly diagnosed localized Ewing sarcoma.

We may cover Fulphila® (pegfilgrastim-jmdb), Ziextenzo ™ (pegfilgrastim-bmez), and Neulasta (pegfilgrastim) for the following indications by growth factor type when the requirements below are met:

1. Acute lymphocytic leukemia (ALL)
   a. After start of induction or first post-remission chemotherapy course
2. Hematopoietic stem cell transplant
   a. To promote bone marrow myeloid recovery, OR
   b. To treat delayed or failed engraftment
3. Myelodysplastic syndrome (MDS)
   a. To treat recurrent infection, OR
   b. To treat neutrophil count < 500 mm$^3$
4. Radiation exposure
   a. After accidental or intentional body irradiation of doses greater than 2 Gy (hematopoietic syndrome of acute radiation syndrome)
5. Support for dose dense chemotherapy in ANY of the following scenarios:
   a. Adjuvant treatment of high-risk breast cancer with combination therapy that includes anthracycline (doxorubicin or epirubicin)/cyclophosphamide followed by paclitaxel, OR
   b. High-dose intensity methotrexate, vinblastine, doxorubicin, and cisplatin (HD-M-VAC) in urothelial cancer; OR
   c. Chemotherapy intensification for newly diagnosed localized Ewing sarcoma.

We may cover Leukine® (sargramostim) for the following indications by growth factor type when the requirements below are met:

1. Acute lymphocytic leukemia (ALL)
   a. After start of induction or first post-remission chemotherapy course
2. Acute myeloid leukemia (AML)
   a. After induction, reinduction, for individuals over 55 years of age
3. Hematopoietic stem cell transplant
   a. To promote bone marrow myeloid recovery, OR
   b. To treat delayed or failed engraftment, OR
   c. To mobilize stem cells for collection by pheresis
4. Myelodysplastic syndrome (MDS)
   a. To treat recurrent infection, OR
   b. To treat neutrophil count < 500 mm$^3$
5. Radiation exposure
   a. After radiation therapy in the absence of chemotherapy, if prolonged delays are expected; OR
b. After accidental or intentional body irradiation of doses greater than 2 Gy (hematopoietic syndrome of acute radiation syndrome)

6. Support for dose dense chemotherapy in **ANY** of the following scenarios:
   a. Adjuvant treatment of high-risk breast cancer with combination therapy that includes anthracycline (doxorubicin or epirubicin)/cyclophosphamide followed by paclitaxel, **OR**
   b. High-dose intensity methotrexate, vinblastine, doxorubicin, and cisplatin (HD-M-VAC) in urothelial cancer; **OR**
   c. Chemotherapy intensification for newly diagnosed localized Ewing sarcoma.

The use of multiple WBC growth factor agents for prophylaxis and/or adjunctive treatment within a given chemotherapy cycle is **NOT clinically indicated**.

We do not cover the medications listed above for other conditions not listed above.

**Requesting Prior Authorization Information through Carelon Medical Benefits Management:**
Prior Authorization will be required when the medications are administered using a member's medical benefit in these settings:
- A clinician's or physician's office
- A home health care provider
- Outpatient hospital and dialysis settings
- Surgical day care.

To request prior authorization for the following products: Commercial Managed Care (HMO and POS), Commercial PPO/EPO and Medicare Advantage (HMO Blue and PPO Blue) please see instructions below.

1. Through the Blue Cross Blue Shield of Massachusetts website:
   - Log in to your Blue Cross Blue Shield of Massachusetts Provider Central account at [www.bluecrossma.com/provider](http://www.bluecrossma.com/provider).
   - Click eTools> Carelon Medical Benefits Management
   - Press Go Now

2. Going directly to Carelon's ProviderPortalSM (registration required)
   - Go to [www.providerportal.com](http://www.providerportal.com)
   - Or calling 1-866-745-1783 (when applicable).

**Requesting Prior Authorization Information through BCBSMA under Retail/Specialty Pharmacy:**
- All requests for outpatient retail pharmacy for indications listed and not listed on the medical policy guidelines may be submitted to BCBSMA Clinical Pharmacy Operations by completing the Prior Authorization Form on the last page of this document.
- Physicians may also call BCBSMA Pharmacy Operations Department at (800) 366-7778 to request a prior authorization/formulary exception verbally. Patients must have pharmacy benefits under their subscriber certificates.

**Sources of Clinical Criteria for Review of Requests for Medicare**
When considering the multiple sources of clinical criteria for review of requests for Medicare Advantage members, Carelon utilizes the following hierarchy to prioritize the criteria applicable to a given request:
- **First:** National Coverage Determinations and other CMS guidance (e.g., Medicare Policy Benefit Manual, Medicare Managed Care Manual, Medicare Claims Processing Manual, and the Medicare Learning Network).
- **Second:** Local Coverage Determinations: If there is no NCD, the clinical reviewers shall apply any applicable LCD. If there is an NCD but also a more specific LCD, then the LCD should be used to determine medical necessity of the request. Any LCAs containing reasonable and medically
necessary indications for a particular item or service will be used along with their associated LCDs in order to make a determination.

- **Third: Health Plan Medical Policy:** If there is no applicable Coverage Determination, the clinical staff will apply any applicable Health Plan Medical Policy.
- **Fourth: Evidence-Based Medical Necessity Criteria:** In the absence of any of the above criteria or where the existing guidance provides insufficient clinical detail to help ensure that all approved services are reasonable and necessary, the physician reviewer will make a determination of medical necessity using objective, evidence-based criteria. Carelon Guidelines is an internal resource available for commonly requested services.

**Individual Consideration**
All our medical policies are written for the majority of people with a given condition. Each policy is based on medical science. For many of our medical policies, each individual’s unique clinical circumstances may be considered in light of current scientific literature. Physicians may send relevant clinical information for individual patients for consideration.

**CPT Codes / HCPCS Codes / ICD Codes**
The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

**CPT Codes**
There is no specific CPT code for this service.

**Policy History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/2023</td>
<td>Reformatted Policy.</td>
</tr>
<tr>
<td>3/2023</td>
<td>Updated AIM’s new name to Carelon.</td>
</tr>
<tr>
<td>2/2023</td>
<td>Updated to add Stimufend ® to the policy.</td>
</tr>
<tr>
<td>1/2023</td>
<td>Updated to add Rolvedon ™ to the policy.</td>
</tr>
<tr>
<td>11/2022</td>
<td>Updated to add Fylmetra ® to the policy.</td>
</tr>
<tr>
<td>10/2022</td>
<td>Updated to add a note that Donor requests will come to Blue Cross.</td>
</tr>
<tr>
<td>7/2022</td>
<td>Updated to add Ziextenzo ™, and Neulasta ® / OnPro ® to preferred also to move Udenyca ™ to non-preferred.</td>
</tr>
<tr>
<td>4/2022</td>
<td>Updated to add Releuko (filgrastim) as non-preferred.</td>
</tr>
<tr>
<td>6/2021</td>
<td>Special early launch of the new policy implemented for colony stimulating factor agents to align with Quality Care Cancer Program (Medical Oncology). Effective 7/1/2021.</td>
</tr>
</tbody>
</table>

**References**


27. Stimufend [Product Information]. Lake Zurich, IL. Fresenius Kabi USA, LLC.; Sept 15, 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761173Orig1s000correctedlbl.pdf Accessed on January 26, 2023

To request prior authorization using the Massachusetts Standard Form for Medication Prior Authorization Requests (eForm), click the link below: http://www.bluecrossma.com/common/en_US/medical_policies/023%20Form%20medication%20prior%20auth%20instruction%20prn.pdf